



CLINICAL STUDY RESULTS

A study to learn about the long-term safety of tazemetostat in people with cancer

Tazemetostat has been withdrawn from the markets due to a safety concern based on findings from another study.

The results of this present study are presented below in the safety section. The results shown in this summary represent one clinical study. Other clinical studies may produce different results.

What was the study about?

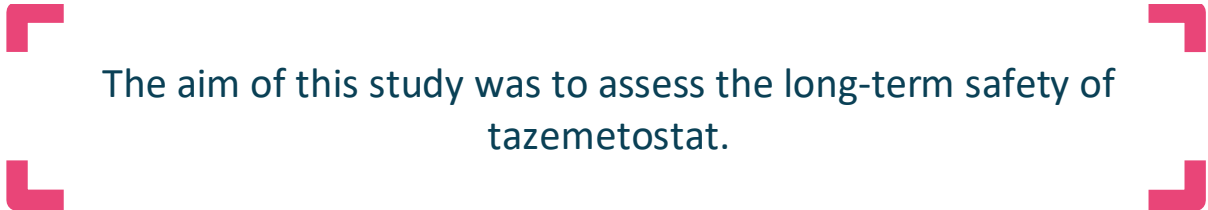
The purpose of this study was to learn about the long-term safety of tazemetostat in people with cancer who were treated with tazemetostat in previous clinical studies were moved to this study to continue receiving tazemetostat.

Tazemetostat works by blocking a protein called EZH2. This protein can help some cancer cells grow. By stopping EZH2, tazemetostat may slow down or stop cancer growth.

Several studies were conducted earlier to see if tazemetostat was safe and was having a medical benefit on people taking it. EZH-501 is a roll-over study. A roll-over study allows participants who have completed an earlier clinical study to continue receiving a treatment that is helping them, while researchers collect additional long-term safety information. Participants joined this roll-over study EZH-501 after completing a previous tazemetostat study.

This study also allowed doctors to collect information on how people did over a long treatment period. People who were previously treated with tazemetostat and tolerated it without unacceptable medical problems and had already benefited from the treatment with no evidence of worsening of their cancer could join this study for continued treatment and follow-up.

As EZH-501 was a roll-over study, no new participants were expected to join. Only participants from earlier tazemetostat studies could enrol and continue treatment. As the number of participants eligible to join this study was reached, the sponsor decided to stop enrolment of more participants and stopped the study early.



The aim of this study was to assess the long-term safety of tazemetostat.

The study took place between August 2016 and September 2025 at 30 study sites in United States, Europe (Belgium, France, Poland, Great Britain, Ukraine) and Australia.

Who took part in this study?



58

PARTICIPANTS



36

MEN



22

WOMEN



61 YEARS
AVERAGE
AGE

To take part in the study, participants had to:



- be benefiting from or getting better with tazemetostat treatment in their previous study.
- be taking tazemetostat alone or with other medicines or having completed the treatment in previous study. Participants receiving tazemetostat with other medicines must have completed the combination treatment in the previous study or were able to continue receiving the other medicine outside of the study.
- have blood test results, kidney function and liver function that met the study requirements for treatment set by the previous study.

Participants could not take part in the study if:



- they had cancer other than the one for which they are receiving tazemetostat.
- they had a health condition(s) or had received treatment(s) that could affect their participation in the study.

What treatments were used in this study?



Study Treatment

Tazemetostat was taken as a tablet by mouth twice a day, in 28-day treatment cycles.

The dose of tazemetostat participants took depended on the previous study they were in.

This was an “open-label”, “roll-over” study. Open-label means that the researchers and the participants knew which treatment was given to each participant. ‘Roll-over’ means people who benefited in a previous study could continue to receive the treatment in the new study without a break.

This study had 3 parts:

Screening: The study doctor checked if participants could take part in this study.

Treatment:

In this study, participants either:

- continued taking tazemetostat as in their previous study if it was still helping them, or
- stopped treatment and continued being followed by the study team to monitor their health and survival.

Participants continued taking tazemetostat as long as it benefited them. They stopped the treatment when their cancer got worse, had medical problems which became too serious, the study doctor decided to stop the treatment, or the participant chose to leave the study.

During the treatment, participants had to visit the study site at least every 3 months or as per the doctor's decision.

Follow-up:

After the last dose of tazemetostat, participants had a final study visit within 1 month, or sooner if they began a new cancer treatment.

The researchers monitored the health of the study participants through a phone call, by checking their medical records, and/or visit to the study site every 3 months, or more often if needed after the last treatment. This follow-up continued until the participant either passed away, could not be reached, or the study was stopped by the company running the study (called the sponsor), whichever happened first.

As EZH-501 was a roll-over study, no new participants were expected to join. Only participants from earlier tazemetostat studies could enroll and continue treatment. As the number of participants eligible to join this study was reached, the sponsor decided to stop enrolment of more participants and stopped the study early. This decision was related to the study design. Participants who were still benefiting from treatment were able to continue receiving tazemetostat through a separate access pathway without interruption.

Screening visit	Treatment period	Follow-up
Participants from the previous studies of tazemetostat could take part in this study. During the first visit, the study doctors checked if each person met the study rules to see if they could join the study.	- Participants either kept taking the study treatment as in their previous study or stopped and were monitored to check their health and survival. - They took tazemetostat until their disease worsened, serious side effects appeared, the doctor decided to stop, or they chose to leave. - While on treatment, participants visited the clinic at least every 3 months or as the doctor recommended.	- Within 1 month after last dose or before starting a new treatment, participants had health check. - Participants were followed up every 3 months through a phone call, by checking their medical records, and/or study site visit. - Follow-up continued until a participant either passed away, could not be reached, or study was stopped early.

What did researchers find out in the study?

The adverse events seen in this study were generally similar to those already known for tazemetostat. Researchers did not identify any new safety concerns in EZH-501.

However, an increased risk of developing certain blood cancers was observed.

What could be learnt about the long-term safety of tazemetostat?

During the study, participants were asked to report any 'adverse events', that is, if they felt unwell, experienced any kind of medical event, or noticed anything different about their bodies. Researchers recorded all adverse events reported by participants, whatever the cause. For example, if some participants caught COVID-19, this was reported as an adverse event, although it was not related to the study treatment.

If the study doctor thinks an adverse event may be related to the study treatment, it is called a 'side effect'. A side effect is considered 'serious' when it is life-threatening, causes lasting problems, or leads to hospitalisation.

In this study, 57 out of 58 participants received tazemetostat. One participant had joined for safety follow-up and did not receive any treatment in this study. These 57 participants were divided into 3 groups based on the dose they received:

- **600 mg or less tazemetostat (13 participants)**
- **800 mg tazemetostat (41 participants)**
- **1200 mg tazemetostat (3 participants)**

Researchers analysed the different dose groups separately because adverse events can sometimes differ depending on the dose received.

Overall, 96% (55 out of 57 participants) reported adverse events. The largest number of adverse events was reported in the 800 mg group. However, this group also included most of the participants in the study, making direct comparisons between groups difficult. The 1200 mg group included only a few participants, therefore the results for this group are more difficult to interpret.

The most commonly reported adverse events that happened in more than 15% of total participants are shown below, both as a percentage (%) followed by the actual number of participants in the group (e.g., 7% or 1 out of 15).

Adverse events	600 mg or less tazemetostat (13 Participants)	800 mg tazemetostat (41 Participants)	1200 mg tazemetostat (3 Participants)	Total participants (57 participants)
Any adverse event	100% (13 out of 13) 	95% (39 out of 41) 	100% (3 out of 3) 	96% (55 out of 57) 
Feeling tired	38% (5 out of 13) 	27% (11 out of 41) 	100% (3 out of 3) 	33% (19 out of 57) 
Low number of red blood cells	23% (3 out of 13) 	20% (8 out of 41) 	67% (2 out of 3) 	23% (13 out of 57) 
Feeling sick (the desire to vomit)	8% (1 out of 13) 	20% (8 out of 41) 	67% (2 out of 3) 	19% (11 out of 57) 
Cough	8% (1 out of 13) 	20% (8 out of 41) 	33% (1 out of 3) 	18% (10 out of 57) 
Infection of the main airways of the lungs	23% (3 out of 13) 	17% (7 out of 41) 	0% (0 out of 3) 	18% (10 out of 57) 
Diarrhoea	15% (2 out of 13) 	17% (7 out of 41) 	0% (0 out of 3) 	16% (9 out of 57) 
Hair loss	23% (3 out of 13) 	15% (6 out of 41) 	0% (0 out of 3) 	16% (9 out of 57) 
High blood pressure	15% (2 out of 13) 	15% (6 out of 41) 	33% (1 out of 3) 	16% (9 out of 57) 

The most commonly reported serious adverse events that happened in 2 or more of total participants are shown below.

Serious adverse events	600 mg or less tazemetostat (13 Participants)	800 mg tazemetostat (41 Participants)	1200 mg tazemetostat (3 Participants)	Total participants (57 participants)
Any serious adverse event	31% (4 out of 13) 	51% (21 out of 41) 	67% (2 out of 3) 	47% (27 out of 57) 
A problem where bone marrow does not make healthy blood cells	0% (0 out of 13) 	7% (3 out of 41) 	33% (1 out of 3) 	7% (4 out of 57) 
Body's extreme response to an infection	8% (1 out of 13) 	0% (0 out of 41) 	33% (1 out of 3) 	4% (2 out of 57) 
Brain stroke	0% (0 out of 13) 	2% (1 out of 41) 	33% (1 out of 3) 	4% (2 out of 57) 
Cancer pain	0% (0 out of 13) 	5% (2 out of 41) 	0% (0 out of 3) 	4% (2 out of 57) 
Loss of fluid from the body	8% (1 out of 13) 	2% (1 out of 41) 	0% (0 out of 3) 	4% (2 out of 57) 
Water on the lungs	0% (0 out of 13) 	5% (2 out of 41) 	0% (0 out of 3) 	4% (2 out of 57) 

Certain adverse events were also closely monitored because they are of special interest for tazemetostat treatment.

The most commonly reported adverse events of special interest that happened in 2 or more of total participants are shown below.

Adverse events of special interest (AESI)	600 mg or less tazemetostat (13 Participants)	800 mg tazemetostat (41 Participants)	1200 mg tazemetostat (3 Participants)	Total participants (57 participants)
Sponsor-defined AESI	15% (2 out of 13)	24% (10 out of 41)	33% (1 out of 3)	23% (13 out of 57)
A problem where bone marrow does not make healthy blood cells	0% (0 out of 13)	12% (5 out of 41)	33% (1 out of 3)	11% (6 out of 57)
A fast-growing blood cancer that starts in the bone marrow and affects the body's ability to make healthy blood cells	8% (1 out of 13)	2% (1 out of 41)	0% (0 out of 3)	4% (2 out of 57)

How long did the participants live after they started taking tazemetostat treatment in the previous studies?

There were not enough participants or follow-up information to calculate the average survival time. However, people with a type of blood cancer called follicular lymphoma lived for over 8 years on average from the start of tazemetostat treatment in earlier study. People with other solid tumours (cancers that form lumps in organs) lived for more than 2 years on average from the start of tazemetostat treatment in earlier study. This study did not compare tazemetostat with another treatment, so researchers could not say whether tazemetostat helped people live longer.

How did the treatment make participants feel?

This section only displays the side effects that were reported during the study. The websites listed at the end of this summary may have more information about the adverse events that happened in this study.

- 11% (6 out of 57 participants) in this study experienced a serious side effect.
- 19 participants died in this study.
 - 3 participants died due to side effects including:
 - a type of blood cancer where the body makes abnormal white blood cells called monocytes (1 participant)
 - a new or different cancer (1 participant)
 - body's extreme response to an infection (1 participant)
 - 2 participants died following adverse events that their respective treating physicians determined were unrelated to the study treatment including:
 - a type of stroke caused by reduced blood flow to the brain (1 participant)
 - a fast-growing blood cancer that starts in the bone marrow and affects the body's ability to make healthy blood cells (1 participant)
 - 6 deaths were reported due to worsening of disease being studied.
 - 2 deaths were reported as due to other causes.
 - 6 deaths were caused by reason unknown.

Overall, 74% (42 out of 57 participants) experienced a side effect:

- **77% (10 out of 13 participants)** who received **600 mg or less tazemetostat**
- **71% (29 out of 41 participants)** who received **800 mg tazemetostat**
- **100% (3 out of 3 participants)** who received **1200 mg tazemetostat**

14% (8 out of 57 participants) permanently stopped taking tazemetostat in the study because of a side effect.

For each serious side effects, no more than 1 participant experienced that side effect in each dose group. These serious side effects were:

- A blood disorder causing an abnormally high number of platelets in the blood
- A problem where bone marrow does not make healthy blood cells
- A type of blood cancer where the body makes immature white blood cells called lymphocytes
- A type of blood cancer where the body makes abnormal white blood cells called monocytes
- Bleeding in the lower part of the gut
- Blood clots formed in veins near your skin
- Body's extreme response to an infection
- Decrease in cells that help the blood to clot
- Fainting
- Inflammation in the gut
- Low number of red blood cells

The most commonly reported side effects that happened in more than 5% of total participants are shown below.

Side Effects	600 mg or less tazemetostat (13 Participants)	800 mg tazemetostat (41 Participants)	1200 mg tazemetostat (3 Participants)	Total participants (57 participants)
Side effect	77% (10 out of 13) 	71% (29 out of 41) 	100% (3 out of 3) 	74% (42 out of 57) 
Feeling tired	23% (3 out of 13) 	22% (9 out of 41) 	67% (2 out of 3) 	25% (14 out of 57) 
Hair loss	23% (3 out of 13) 	12% (5 out of 41) 	0% (0 out of 3) 	14% (8 out of 57) 
Low number of white blood cells that fight infection	15% (2 out of 13) 	10% (4 out of 41) 	0% (0 out of 3) 	11% (6 out of 57) 
Decrease in cells that help the blood to clot	8% (1 out of 13) 	7% (3 out of 41) 	67% (2 out of 3) 	11% (6 out of 57) 
Low number of red blood cells	0% (0 out of 13) 	12% (5 out of 41) 	33% (1 out of 3) 	11% (6 out of 57) 
Weakness	0% (0 out of 13) 	12% (5 out of 41) 	0% (0 out of 3) 	9% (5 out of 57) 
Altered sense of taste	0% (0 out of 13) 	7% (3 out of 41) 	33% (1 out of 3) 	7% (4 out of 57) 
Diarrhoea	8% (1 out of 13) 	7% (3 out of 41) 	0% (0 out of 3) 	7% (4 out of 57) 
Feeling sick (the desire to vomit)	0% (0 out of 13) 	5% (2 out of 41) 	67% (2 out of 3) 	7% (4 out of 57) 
Infection of the main airways of the lungs	0% (0 out of 13) 	10% (4 out of 41) 	0% (0 out of 3) 	7% (4 out of 57) 

A problem where bone marrow does not make healthy blood cells	0% (0 out of 13) 	5% (2 out of 41) 	33% (1 out of 3) 	5% (3 out of 57) 
Muscle cramps	0% (0 out of 13) 	7% (3 out of 41) 	0% (0 out of 3) 	5% (3 out of 57) 

More information

To learn more about this study, please visit:

- ClinicalTrials.gov and search for study NCT02875548 or
- Clinicaltrialsregister.eu/ctr-search/search and search for study 2015-004984-35 or
- Search for clinical trials - EMA (euclinicaltrials.eu) and search for study 2023-510553-41-00.

For more information about current treatments available, please speak to your healthcare provider. If you have any questions about this study, please contact the sponsor, Ipsen at:



clinical.trials@ipson.com

Future research

Tazemetostat was taken off the market in March 2026 because of safety concerns found in a separate clinical study, not in this study. Because of this, no further studies with tazemetostat are planned.

Study identification and other information

FULL STUDY TITLE: Tazemetostat rollover study (TRUST): an open-label, rollover study

STUDY NUMBERS: Europe: 2023-510553-41-00 | United States: NCT02875548 |

PROTOCOL: EZH-501.

OTHER INFORMATION: Phase I and II rollover studies can take several months to years to complete. Analysis of the study results show how safe and/or effective a study treatment was during the study.



We sincerely thank all the participants who took part in this study. Without their contribution, advances in medical research would not be possible.

We also thank the patient representatives who reviewed this summary and provided valuable feedback to help make it clearer and easier to understand for a general audience.

